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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,064	04/20/2005	Scott Alan Jelinksy	AM100877	8561

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WYETH
PATENT LAW GROUP
5 GIRALDA FARMS
MADISON, NJ 07940

EXAMINER	
LUNDGREN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 10/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/511,064	JELINKSY ET AL.	
	Examiner	Art Unit	
	Jeff Lundgren	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *6 and 8-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *see office action*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-58 are pending in the instant application, with claims 10-59 withdrawn as being directed to a non-elected invention and claims 6, 8 and 9 withdrawn as being directed to a non-elected species. Claims 1-5 and 7 stand rejected, and are the subject of the Office Action below.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 23, 2006, has been considered by the Examiner. The submission is in compliance with the provisions of 37 CFR § 1.97. Enclosed with this Office Action is a return-copy of the Form PTO-1449 with the Examiner's initials and signature indicating those references that have been considered.

Withdrawn Rejections

Claim Rejections - 35 USC § 101

The rejection of the claims under 35 U.S.C. § 101, is withdrawn in view of Applicants' amendments to the claims.

Maintained Rejections

Claim Rejections - 35 USC § 112, first paragraph (Written Description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-5 and 7 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The written description requirement is distinct from the enablement requirement; this was first pointed out by the court in *In re Ruschig*, 379 F.2d 990, 154 USPQ 118 (CCPA 1967), and

clarified in *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). The issue of whether the claimed subject matter is adequately supported/described by the specification, is a question of fact. *Id.* at 1563, 19 USPQ2d at 1116.

When considering whether the claimed subject matter complies with the written description requirement, Applicants' disclosure should be read in light of the knowledge possessed by those skilled in the art.

> "[T]he disclosure in question must be read in light of the knowledge possessed by those skilled in the art, and that knowledge can be established by affidavits of fact composed by an expert, and by referencing to patents and publications available to the public..."

In re Lange, 644 F.2d 856, 863, 209 USPQ 288, 294 (CCPA 1981). *See also, In re Alton*, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

Applicants enjoy the presumption that their patent application is valid and all statements contained therein are accurate; it is the PTO's burden to demonstrate why any of Applicants claims should be rejected or why any of Applicant's statements should be doubted.

> "it is incumbent upon the Patent Office, whenever a rejection... is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure."

In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The court has made it clear that such challenges apply to written description rejections:

> "we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."

In re Wertheim, 191 USPQ 90, 97 (CCPA 1976).

If the PTO is successful in presenting such evidence and argument, the burden then shifts to the Applicant to provide evidence that would convince one to the contrary that the disclosure as a whole provides written description support for the claimed subject matter.

The Claimed Invention

Applicants' claimed invention is directed to *all combinations* of isolated gene sets of a first and second groups, wherein each gene in the first group is differentially expressed at higher levels in kidney upon estrogen exposure, and wherein each gene in the second group is differentially expressed at lower levels in kidney cells upon estrogen exposure. Effectively, all isolated combinations of estrogen-responsive kidney genes and fragments thereof. The claimed "estrogen" is a class of estrogen compounds, not a single compound, and includes compounds such as 17-beta estradiol (for example, see page 21, second paragraph).

The Supporting Disclosure

In the *Background of the Invention* (pages 1-3), Applicants summarize the roles of estrogens on various organs of the human body and certain pathologies associated with aberrant levels of estrogen, and how the medical community could benefit from having a better understanding of the up- and down-regulated genes in response to estrogen of various organs, including ovary, uterus, bladder and lung.

In the *Summary of Embodiments* (pages 6-9), Applicants indicate that the invention is directed to a plurality of genes in the aforementioned organs in response to certain various hormones, including estrogen-responsive kidney genes, and the use of such genes for identifying various pathological conditions.

In the *Detailed Description of the Invention*, Applicants provide certain description: definitions related to the claimed invention and other inventive embodiments (pages 9-20); description of general laboratory techniques used in molecular cloning, including certain techniques related to differential expression analysis, including general descriptions for obtaining the biological samples and assays (page 21), certain gene measurements and statistical procedures (page 23 and 24); a certain plurality of genes allegedly responsive to estrogen (pages 25-27); methods of identifying "agents" (pages 27 and 28); general pharmaceutical and methods of various treatments (pages 29-34); and methods of monitoring and kits that are either directly or indirectly related to the claimed invention (pages 34 and 35). Applicants provide a limited number of examples directed toward determining certain genes in certain tissues, including the kidney, that are responsive to estrogen. Applicants describe the selection of the animal and its

handling (page 36); the use of a gene microarray (pages 36 and 37); data selection and analysis (page 37 and 38); and the discussion of certain results related to various organs, including the kidney (pages 38-44).

The State of the Art, Relevant Facts and Applicants Lacking Disclosure

As it is with many biotechnology inventions, the relevant art is multidisciplinary. Applicants' claimed invention relates to a number of core technologies and scientific concepts including polymerase chain reaction biochemistry, DNA microarrays, instrumental analysis, pathology, endocrinology and bioinformatics, to name a few. Accordingly, those of skill in the art have a firm understanding of the inter-relationship between each of the disciplines and the functional and physical limitations of the claimed invention, and is pertinent in determining the level of skill in the art.

Taken as a whole, the relevant art suggests that Applicants were neither in possession nor had written description support for their claimed invention at the time the application was filed. When compared with Applicants' lacking disclosure, a number of art-related references support this finding, for example, Chern *et al.*, *Nephron 85*:258-266 (**2000**), and Kuiper *et al.*, *Frontiers in Neuroendocrinology 19*:253-286 (**1998**).

As mentioned previously, the claims are directed to a plurality of any and all "genes" that are differentially expressed in kidney cells when exposed to estrogen. However, Applicants' disclosure only has limited support for the range of genes that appear to be differentially expressed, and only in response to a limited number of number or agents.

For example, Chern explains the difficulty in providing a full set of differentially expressed kidney genes, an embodiment encompassed by Applicants' claims:

> "Differential hybridization of ordinary cDNA libraries using total cDNA probes can only identify the abundant or moderately abundant genes differentially expressed. The method is not sensitive enough to isolate those genes expressed rarely and differentially [21]. We have screened by differential hybridization about 100,000 clones of an ordinary rat kidney cDNA library constructed in this laboratory and could not isolate any other genes differentially expressed between SHR and WKY (unpublished data)."

Chern, page 259.

Additionally, Kuiper provides a detailed review of estrogen receptors, such as ERα and ERβ, in certain tissues, including the kidney. Kuiper summarizes that:

> "Ligand-binding experiments have shown specific binding of 17b-estradiol by ERβ with an affinity similar to that of ERα. The rat tissue distribution and/or the relative level of ERα and ERβ expression seems to be quite different, i.e., moderate to high expression in uterus, testis, pituitary, ovary, kidney, epididymis, and adrenal for ERα and prostate, ovary, lung, bladder, brain, bone, uterus, and testis for ERβ. Within the same organ it often appears that the ER subtypes are expressed in different cell types, supporting the hypothesis that the ER's may have different biological functions. The cell type-specific expression of ERα and ERβ in rat prostate, testis, uterus, ovary, and brain and the distribution of ERβ mRNA in the ERα knock-out mouse brain are discussed. The discovery of ERβ suggests the existence of two previously unrecognized pathways of estrogen signalling; via the ERβ subtype in tissues exclusively expressing this subtype and via the formation of heterodimers in tissues expressing both ER subtypes. The existence of two ER subtypes, their differential expression pattern, and different actions on certain response elements could provide explanations for the striking species-, cell-, and promoter-specific actions of estrogens and antiestrogens."

Abstract, page 253.

Accordingly, there appears to be no reasonable evidence to the contrary of that would lead one of ordinary skill in the art to believe that Applicants' had possession of the full scope of the claimed invention.

Accordingly, none of the claims have written description support.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 7, are rejected under 35 U.S.C. 102(b) as being anticipated by Ecker *et al.*, U.S. Patent No. 5,747,253, issued on May 5, 1998.

Claim 1 is directed to an isolated plurality of genes, wherein the plurality comprises two groups of genes, wherein each gene in the first group is differentially expressed at higher levels in kidney upon estrogen exposure, and wherein each gene in the second group is differentially expressed at lower levels in kidney cells upon estrogen exposure. It is noted that Applicants define gene in the specification as follows:

> "In general, 'a gene' is a region on the genome that is capable of being transcribed to an RNA that either has a regulatory function, a catalytic function and/or encodes a protein. A gene typically has introns and exons, which may organize to produce different RNA splice variants that encode alternative versions of a mature protein. ***'Gene' contemplates fragments of genes that may or may not represent a functional domain***."

Specification, paragraph 0042 (emphasis added).

Ecker teaches the use of all possible 8-mer DNA probes (*i.e.*, gene fragments):

> "A group of 65,536 unique 8-mers in 4 sets of 16,348 was prepared in accordance with Examples 3 and 6 each was screened for activity against human herpes simplex virus type 1 (HSV-1) in cell culture in accordance with the procedure described in Example 9. As illustrated in Table 4, antiviral activity was observed with increasing potency at each round of synthesis and screening, with no difficulty discerning the most active set (in bold) in each round."

Ecker, see Example 13, cols. 19 and 20.

Accordingly, Ecker teaches all possible genes (*i.e.*, gene fragments), and therefore metes the limitation of an isolated plurality of "genes" comprising two groups: the first group comprising "genes" expressed at higher levels in kidney cells upon exposure to estrogen (including all 8-mers of NTT73, CYP7B1 and ABCC3), and the second group comprising "genes" expressed at lower levels in kidney cells upon exposure to estrogen (including all 8-mers of SAHH and BHMT).

Conclusions

No claim is allowable.

Applicant's' amendments necessitated the new ground of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

PETER PARAS, JR.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600